201-15840

HIGH PRODUCTION VOLUME (HPV) CHEMICAL CHALLENGE PROGRAM

TEST PLAN
For
Tris(2-chloroethyl) Phosphite
(T2CEP)
CAS No. 140-08-9

Submitted to the US EPA
By
Rhodia Inc.

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1 INTRODUCTION

Under the U.S. Environmental Protection Agency (EPA) High Production Volume (HPV) Challenge Program, Rhodia Inc. (formerly Albright and Wilson Americas Inc.) voluntarily committed to compile a basic screening data on:

- **CAS# 140-08-9, Tris(2-chloroethyl) phosphite (T2CEP)**

This test plan follows up on that commitment. Specifically, this test plan sets forth how Rhodia intends to address testing information for Tris(2-chloroethyl) phosphite, commonly referred to as T2CEP. The test plan reflects that T2CEP is used as a chemical intermediate in closed systems with minimal opportunity for worker exposure and environmental releases during normal handling. A reduced testing program, required for closed system intermediates, is proposed on this basis.

In preparing this test plan the following steps were undertaken:

Step 1: A search was conducted for relevant published and unpublished literature on T2CEP

Step 2: The compiled data was evaluated for adequacy in accordance with EPA guidance documentation.

2 GENERAL SUBSTANCE INFORMATION

Chemical name: Tris(2-chloroethyl) phosphite

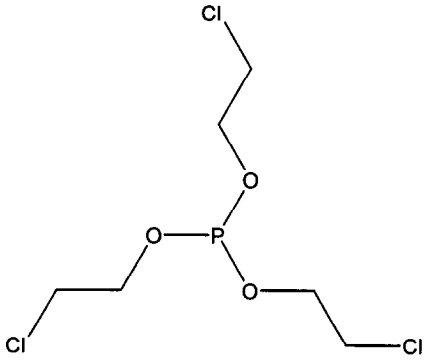
CAS No: 140-08-9

Synonyms: Ethanol, 2-chloro-, phosphite (3:1) - 2-chloroethanol phosphite (3:1) - Ethanol, 2-chloro-, phosphite - Phosphorous acid, tris(2-chloroethyl) ester - Tri(2-chloroethyl) phosphite - Tris(2-chloroethyl) phosphite - Tris(2-chloroethyl)ester of phosphorous acid - Tris(b-chloroethyl) phosphite - Tris(chloroethyl) phosphite- T2CEP

Molecular formula: $C_6H_{12}Cl_3O_3P$

Molecular weight: 269.49

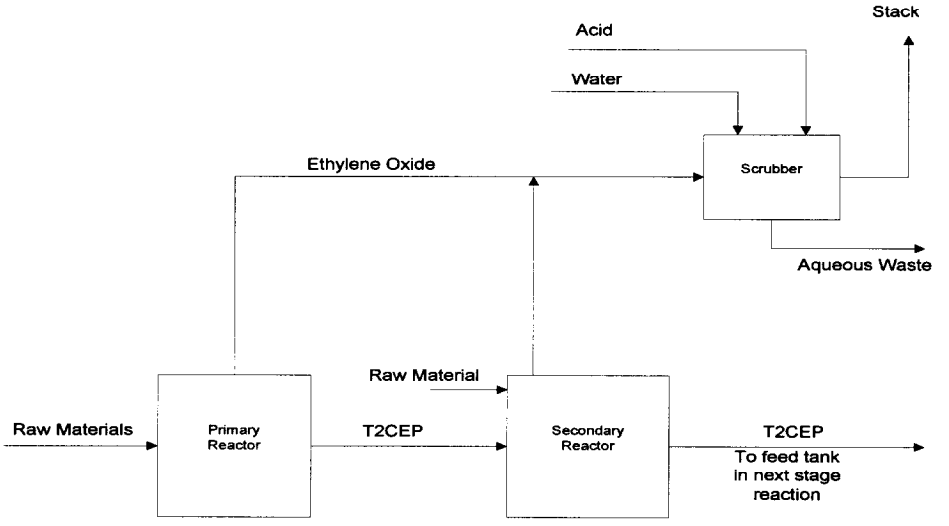
Structural diagram:



3 USE AND EXPOSURE INFORMATION

This substance is manufactured by a single US producer, Rhodia Inc., at a single manufacturing site. T2CEP is used almost exclusively as a chemical intermediate in production of another chemical at the same production facility. T2CEP is handled as a closed system intermediate.
The T2CEP production process is a site limited, continuous closed system process, involving a primary and secondary reactor connected by enclosed steel pipework (See Figure 1). T2CEP exiting the secondary reactor is piped directly into a 600 gallon feed tank, which continuously feeds T2CEP into the downstream product reactor. The next stage reaction is controlled so that the T2CEP is consumed as it is formed, without the need for additional on-site storage for T2CEP. In the next stage reaction T2CEP is fully converted, leaving only residual traces of T2CEP (<0.3%) in the downstream product. This downstream product is also being assessed in the HPV challenge program, and is also mainly used as a chemical intermediate.

Figure 1: T2CEP Production Flow Diagram



At the production site a small number of plant workers (<5 per shift) are involved in operating the process. Therefore, worker exposure to T2CEP during production is extremely limited. Although no atmospheric monitoring data have been found for T2CEP itself at the production plant, atmospheric monitoring of some of the raw materials such as ethylene oxide have been conducted at the plant and are very low, consistent with a closed system process.

Once or twice each year, a very small volume of T2CEP (about 0.1% of total production) is currently packed into tightly sealed 55 gallon drums. The drumming equipment is equipped with exhaust ventilation and exposure is expected to be minimal. These strictly controlled drum quantities are sold to 1-2 industrial customers. This extremely limited quantity of T2CEP is transported from the plant to a near-by warehouse in trucks. The product and trucks are labeled and marked according to regulatory requirements. From the warehouse the product is shipped to the customer.

The transport of this small quantity is in a closed packaged system with little or no opportunity for exposure or release and, therefore, still meets the HPV requirements of a closed system intermediate. Environmental releases and worker exposure during transport of drums are expected to be negligible under normal circumstances.

4 REVIEW OF EXISTING DATA AND DEVELOPMENT OF TEST PLAN

Rhodia Inc. has undertaken a comprehensive evaluation of all relevant data on the SIDS endpoints of concern for T2CEP.

The most significant and reliable data are gathered in Table n° 2. The availability of the data on the specific SIDS endpoints are summarized in Table n° 3.

4.1 Review of existing physicochemical data and proposed testing

Boiling point values at reduced pressure are available from standard data sources. These values are consistent and one of them is reported in Table n° 2. A specific density value is available from a standard data source and is reported in Table n° 2.

Melting point, vapor pressure, water solubility and octanol/water partition coefficient are estimated with the EPIWIN program, and are reported in Table n° 2.

Therefore, no additional testing is proposed for these endpoints in the purposes of the HPV program.

4.2 Review of existing environmental fate data and proposed testing

- *Photodegradation*

An estimated half-life of 11.7 hours is obtained with the AOP program considering an OH radical concentration of $1.5x10^6$ molecules/cm^3 for 12 hours per day. **Therefore no photodegradation test is proposed for purposes of the HPV program.**

- *Stability in water*

Standard data source indicates that T2CEP hydrolyzes. Indeed other trialkyl phosphites are also known to hydrolyze, and in particular experimental hydrolysis studies of reliability (1) or (2) are available on triethyl phosphite (TEP, CAS 122-52-1). The general hydrolysis reactions for trialkyl phosphites are given below:

$(RO)_3P + H_2O \rightarrow (RO)_2P(O)H + ROH$
$(RO)_2P(O)H + H_2O \rightarrow (RO)P(O)(H)OH + ROH$
$(RO)P(O)(H)OH + H_2O \rightarrow H_3PO_3 + ROH$

However no experimental rate of hydrolysis is available for T2CEP. **Therefore a hydrolysis study according to OECD 111 test guideline is proposed.**

- *Biodegradation*

No experimental data is available on T2CEP biodegradation.

Experimental biodegradability studies of reliability (1) are available on triethyl phosphite (TEP, CAS 122-52-1). TEP is not readily biodegradable, and its biodegradation rate is limited by its rate of hydrolysis.

T2CEP, due to its higher hydrophobicity, is not expected to have a higher rate of hydrolysis than TEP. T2CEP is thus not expected to be readily biodegradable either.

Therefore no ready biodegradation test is proposed for purposes of the HPV program.

– *Transport and distribution*

Level III fugacity modeling shows that T2CEP distributes mainly to water and soil when discharged equally in air, water and soil. When discharged only in water, T2CEP remains in the water compartment. When discharged only in soil, T2CEP remains mainly in soil with a significant transfer to the water compartment. When discharged only in air, significant amounts of T2CEP are transferred to the soil and water compartments.

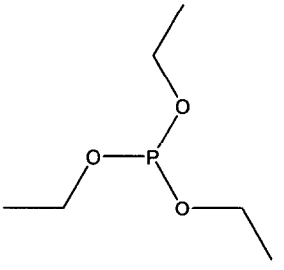
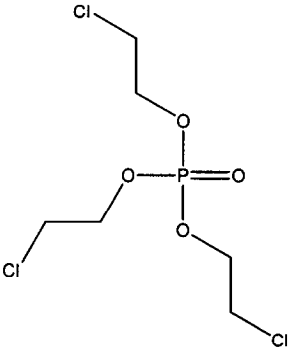
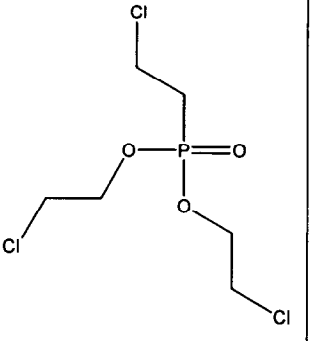
4.3 Review of existing ecotoxicity data and proposed testing

No ecotoxicity data are available on T2CEP.

There are no close analogs of T2CEP, however experimental data of reliability (1) or (2) are available on other substances having either the phosphite moiety (TEP) or the three chloroethyl groups (TCEP, BISCEP).

The table below summarizes the chemical structures and the most relevant ecotoxicity data on these substances:

Table 1: Chemical structures and most relevant ecotoxicity data on TEP, TCEP and BISCEP

End-point	TEP CAS No 122-52-1	TCEP CAS No 115-96-8	BISCEP CAS No 6294-34-4
			
Acute toxicity to fish	96h-LC50 = 252 mg/l	96h-LC50 = 170 mg/:	96h-LC50 > 100 mg/l
Acute toxicity to daphnia	24h-EC50 = 94.1 mg/l	24h-EC50 = 451 mg/l	48h-EC50 = 240 mg/l
Toxicity to algae	72h-EC50 > 73.6 mg/l 72h-NOEC = 37 mg/l	96h-EbC50 = 1.2 mg/l	96h-ErC50 = 73.5 mg/l 14d-NOEC = 18 mg/l

TEP: Triethyl phosphite
TCEP: Tris(2-chloroethyl) phosphate
BISCEP: Bis(2-chloroethyl) 2-chloroethylphosphonate

From this set of data, low acute toxicity of T2CEP towards fish and daphnia is expected. The most sensitive species is most probably algae.

Therefore, an algae toxicity test according to OECD 201 test guideline is proposed to assess the aquatic toxicity of T2CEP.

Review of existing toxicity data and proposed testing

– *Acute oral toxicity*

The acute oral toxicity of T2CEP was evaluated in four studies. These studies were not performed according to Good Laboratory Practices (GLP) but their respective protocols were very similar to OECD guideline 401. The resulting LD50 values ranged from 100 to 370 mg/kg b.w. The lowest value of 100 mg/kg bw was selected as the reference value for T2CEP. Consequently T2CEP is considered as toxic by the oral route. **Therefore, no acute testing is proposed for purposes of the HPV program.**

– *Genotoxicity : Gene mutation*

An Ames test using *Salmonella typhimurium* strains 98, 100, 1535, 1537 and 1538 both with and without metabolic activation (Arochlor-induced rat liver S9 fraction) was performed with T2CEP and showed a negative result. This study was not a GLP study. The only deviation from the OECD guideline 471 consists in the absence of test with *Escherichia coli* WP2 or *S. typhimurium* 102. Nevertheless the results are considered as reliable.

A mammalian cell gene mutation assay was conducted on T2CEP with L5178Y Mouse lymphoma cells TK $^{+/-}$. This study was GLP and fulfilled all of the OECD guideline 476 requirements. The T2CEP concentrations above which cytotoxicity appears were clearly determined. The results were negative, with and without metabolic activation.

– *Genotoxicity : Chromosomal aberration*

A mitotic recombination test was performed with the strain D4 of *Saccharomyces cerevisiae* (a diploid heteroallelic mutant). This study was not GLP but its protocol was very similar to the OECD guideline 481. The reliability score 2 was assigned because the negative results were not confirmed by another study carried out with cells in stationary phase of growth as required by the OECD guideline and because the number of plates/concentration was not reported.
The results were negative with and without metabolic activation.

- Conclusion for the toxicology testing :

T2CEP is a closed system intermediate and consequently a reduced testing is considered:

- The SIDS endpoints concerning the acute toxicity and the genotoxicity are considered as filled adequately.
- According to the EPA document "Guidance for testing closed system intermediates for the HPV challenge program", the tests for repeated dose toxicity and reproductive toxicity are not required.
- **A toxicity test in compliance with the OECD guideline 421 is proposed to fill the developmental toxicity SIDS endpoint.**

5 SUMMARY

In summary, the testing proposed in Table n° 3 will complete the data acquisition requirements for T2CEP under the U.S. Environmental Protection Agency High Production Volume (HPV) Chemical Challenge Program.

6 ROBUST STUDY SUMMARIES

An IUCLID Data Set for T2CEP is appended, including references of all data.

Table n° 2: Significant Data on T2CEP

T2CEP CAS No 140-08-9		
Endpoint	**Result**	**Comment**
Physicochemical		
Melting point	65 °C	Estimation
Boiling point	119 °C at 0.2 hPa	Handbook
Density	1.353 at 20°C	Handbook
Vapor pressure	4.05 x 10^{-4} hPa at 25°C	Estimation
Log Pow	1.51 at 25°C	Estimation
Water solubility	951 mg/l at 25°C	Estimation
Environmental fate and pathway		
Photodegradation	DT50 (in air) = 11.7 h	Estimation
Stability in water	Hydrolyzes	Handbook
Transport/distribution	Air = 0.7% Water = 47.1% Soil = 52% Sediment = 0.1%	Fugacity model level III, discharge in air, water and soil.
Biodegradation	Not expected to be readily biodegradable	Estimation based on data on another substance
Ecotoxicity		
Acute fish	Low toxicity expected	Estimation based on data on other substances
Acute daphnia	Low toxicity expected	
Algae	No data	-
Toxicology		
Acute oral toxicity	LD50 = 100 +/- 15 mg/ kg b.w.	The lowest LD50 among the reliable results.
Repeated dose toxicity	No data	-
Genetic toxicity *In vitro*		
Gene mutation	Ames test : negative	The strains *E. coli* WP2 or *S. typhimurium* 102 were not employed in this test.
	Mammalian cell gene mutation assay (L5178Y mouse lymphoma cells T+/-) : negative	OECD guideline 476. In case of metabolic activation the cytotoxicity of T2CEP was reduced by a 33 factor.
Chromosomal aberration	Mitotic recombination in Saccharomyces cerevisiae D4 : Negative	T2CEP did not increase the frequency of genetic conversion in this diploid heteroallelic mutant strain.
Genetic toxicity *In vivo*	No data	-
Toxicity to reproduction	No data	-
Developmental tox/teratogenicity	No data	-
Human experience	No data	-

Table n° 3 : Availability of data and proposed testing on T2CEP

T2CEP CAS No 140-08-9							
Endpoint	**Available**	**GLP**	**OECD study**	**Other study**	**Estim. method**	**Accept-able**	**SIDS testing required**
Physicochemical							
Melting point	Y	N	N	N	Y	Y	N
Boiling point	Y	N	N	Y	N	Y	N
Density	Y	N	N	Y	N	Y	N
Vapor pressure	Y	N	N	N	Y	Y	N
Oct:water partition coef	Y	N	N	N	Y	Y	N
Water solubility	Y	N	N	N	Y	Y	N
Environmental fate and pathway							
Photodegradation	Y	N	N	N	Y	Y	N
Stability in water	N	-	-	-	-	-	Y
Transport/distribution	Y	N	N	N	Y	Y	N
Biodegradation	N	-	-	-	-	-	N*
Ecotoxicity							
Acute fish	N	-	-	-	-	-	N**
Acute daphnia	N	-	-	-	-	-	N**
Algae	N	-	-	-	-	-	Y
Toxicology							
Acute toxicity	Y	N	N	Y	N	Y	N
Repeated dose toxicity	N	-	-	-	-	-	N
Genetic toxicity : Gene mutation - Bacterial (Ames test)	Y	N	N	Y	N	Y	N
- Mammalian (L5178Y mouse lymphoma cells)	Y	Y	Y	N	N	Y	N
Chromosomal aberration : Mitotic recombination in S. cerevisiae D4	Y	N	N	Y	N	Y	N
Toxicity to reproduction	N	-	-	-	-	-	N
Devel. tox/terat	N	-	-	-	-	-	Y
Human experience	N	-	-	-	-	-	N
Other	N	-	-	-	-	-	N

Y : yes
N : no
** See justification in section 4.2*
*** See justification in section 4.3*